Purpose: Detecting cartilage damage immediately following trauma could allow for early intervention and the subsequent prevention of post-traumatic osteoarthritis (PTOA) development. Current clinical imaging modalities do not have cellular resolution to detect subtle structural changes or chondrocyte viability. Multiphoton microscopy (MPM) can acquire micron resolution structural and biological information in live tissues. The purpose of this study was to utilize MPM imaging with FDA-approved angioscopic fluorescein dye to characterize the viability of early cartilage damage to further understand the early pathophysiology of PTOA.
Methods: Osteochondral blocks from the distal metacarpi of horses aged 4-6 years were placed in a custom-designed holder on an EnduraTEC ELF3200 mechanical test frame (EnduraTEC). The articular surface of each medial condyle was injured with a single compressive load of 30 MPa via a 2.25 mm flat ended cylindrical indenter within 1 sec to model traumatic injury. The lateral condyle served as the control. After 1 hour, blocks were placed in 1 μM fluorescein sodium (AK-FLUOR 25%, Akorn) and imaged with MPM. Emission spectra was collected and quantified using custom image analysis code in MATLAB (MathWorks) to determine chondrocyte viability and spatial distribution.
Results: Within one hour of damage, MPM imaging demonstrated significantly increased chondrocyte death ($p<0.001$, as assayed by dye penetration through ruptured membranes), autofluorescent signatures, and micro-cracks when compared to controls (Figure 1). Reconstructed MPM data revealed that cell death (Figure 2) occurred in either a circular pattern corresponding to a region around the perimeter of the indenter, or in an elliptical pattern (Table 1).
Conclusions: MPM reveals cellular and matrix damage in live cartilage and reveals novel findings relevant to early PTOA pathophysiology. The reconstructed 3-D pattern of death-dissemination and the development of autofluorescent signatures following trauma could serve as optical biomarkers for early PTOA and are below the resolution of other imaging modalities that can be used on live tissue. Adaptation of MPM to in vivo imaging is in progress and has the potential to further elucidate the early events of PTOA.

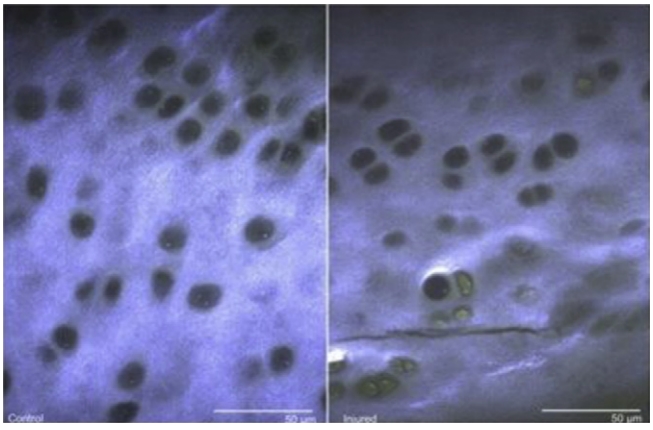

Figure 1. MPM of control and injured samples. Control samples typically contained few fluorescein-stained cells, while injured samples typically contained fluorescein-stained cells, autofluorescent structures, and cracks.

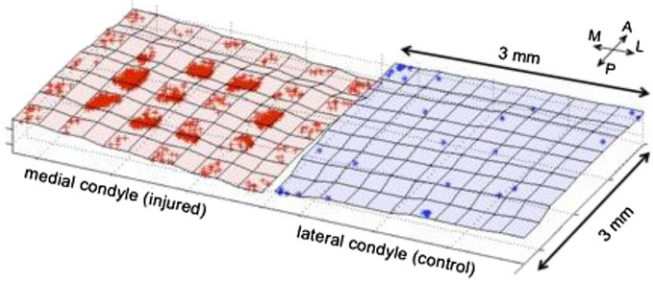

Figure 2. 3-D reconstruction of control and injured cartilage from n=1 sample. Each point represents a single dead chondrocyte. The total volume scanned was a checkerboard of volumetric Z-scans, with 10 images at 10 μm-step intervals. An image such as that in Figure 1 represents 1.6% of the area in Figure 2.

Table 1
Mean peak load (±SE), mean peak displacement (±SE), and mean percent-difference between the long- and short-axis (±SE) in circular (n=7) and elliptical (n=4) damage patterns.

	Load (N)	Displacement (μm)	Axes; Difference (%)
Circular	117.70 ± 0.02	367.1 ± 50.8	15.2 ± 1.8
Elliptical	117.70 ± 0.02	372.5 ± 29.7	74.4 ± 32.7

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RADIOLOGIC PROGRESSION IN HAND OSTEOARTHRITIS (OA) OVER 2.6 YEARS - DATA FROM THE SEKOIA TRIAL

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Purpose: Hand OA is a frequent polyarticular disease. Few is known with respect to its radiological progression over time, which in addition is difficult to assess, considering that no radiographic scoring method has, today, proved being superior to another. The goal of this study was to assess hand OA radiological progression over 3 years using three validated scoring methods.
Methods: Data came from an international 3-year, randomized, placebo-controlled phase III trial designed to assess the effect of strontium ranelate compared to placebo on the radiographic progression of knee OA which included symptomatic primary knee OA patients (ACR criteria) at a Kellgren-Lawrence (KL) grade II or III, with a minimal joint space width (JSW) between 2.5-5 mm. During this trial, baseline and final postero-anterior radiographs of each hand were performed. Symptoms were assessed using the functional index for Hand OA (FIHOA; range 0-30) and the AUSCAN (0-300). Two independent readers scored half of the pairs of radiographs obtained each, blinded to treatment and time sequence, using the KL (range 0-128), Kallman (0-204) and Verbruggen anatomical phase (0-218) scoring methods with a good inter-rater reproducibility. Hand OA radiographic progression was studied in the placebo group by looking at 1/ baseline-end changes in global scores, 2/ the numbers of progressors (progression defined for each global score by a change over each reader's smallest detectable difference (SDD)), and 3/ the number of patients in whom at least 1 joint showed a deterioration (from KL0-1 to KL≥2; progression of ≥1 phase for Verbruggen score).
Results: Of 1669 patients included in the SEKOIA trial, 1371 had baseline hand radiographs of whom 999 had radiologic hand OA: 73%. 297 patients in the placebo group had baseline and post-baseline radiographs. 72% were female, mean age 64±7 years, body mass index 29.5±5 kg/m^2, and initial knee JSW 3.5±0.8 mm. Baseline hand OA radiologic severity was mild: KL score 21±13, Kallman score 24±21 and Verbruggen score 13±14. FIHOA score was 4±5, Auscan global score was 96±80. Mean time interval between baseline and final radiographs was 31.5 months. Hand OA radiographic progression over 2.6 years was modest with a mean change of 2.4±3.3 for KL score, 3.7±5.3 for Kallman score and 2.0±4.0 for Verbruggen score.
The numbers (%) of progressors (change≥SDD) were 7 (2%), 17 (6%), and 21 (7%) respectively.
The numbers (%) of patients with at least 1 worsened joint were 169 (57%) for KL and 139 (47%) for Verbruggen score, with respective means of 2.0±1.3 and 1.7±1.1 worsening joint.
Conclusions: Whatever the radiological scoring method used, and the kind of analysis performed, mild radiographic hand OA patients showed a very weak global radiological progression over 2.6 years. In future structure-modification trials in hand OA, analysing the number of patients with at least one joint worsening could be the most sensitive method.

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RATES AND SENSITIVITY OF KNEE CARTILAGE LOSS IN RADIOGRAPHIC DISEASE STRATA - CENTRAL VERSUS SITE READINGS FROM THE OSTEOARTHRITIS INITIATIVE

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Purpose: Previous studies showed a weak relationship of mild vs. moderate joint space narrowing (specifically OARSI JSN grades 1/2) with knee pain and the body mass index (BMI). In the Osteoarthritis